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Review

Diagnosis and classification of ulcerative colitis

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ABSTRACT

Ulcerative colitis (UC) is a chronic relapsing inflammatory bowel disease (IBD) characterised by superficial mucosal ulceration, rectal bleeding, diarrhoea, and abdominal pain. In contrast to Crohn's disease (CrD), UC is restricted to the colon and the inflammation is limited to the mucosal layer. Classic UC affects the colon in a retrograde and continuous fashion starting from the rectum and extending proximally. Dependent on the anatomic extent of involvement, UC can be classified as proctitis, left-sided colitis, or pancolitis. Inflammatory arthropathies and primary sclerosing cholangitis (PSC) are the most common and clinically most important extraintestinal manifestations of UC. The aetiopathogenesis of UC is incompletely understood, but immune-mediated mechanisms are responsible for dysregulated immune responses against intraluminal antigens in genetically predisposed individuals. The diagnosis is based on the history, as well as clinical, radiological, endoscopic and histological features. Autoantibodies, mainly antineutrophil cytoplasmic antibodies (ANCA) and anti-goblet cell antibodies (GAB) may be helpful in the early diagnosis of UC and in differentiating it from CrD.

Contents

1. Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) characterised by superficial mucosal inflammation, rectal bleeding, diarrhoea, and abdominal pain. In contrast to Crohn's disease (CrD) (see Chapter "Diagnosis and classification of Crohn's disease" in this issue), UC is usually restricted to the colon and the inflammation is limited to the mucosa.

2. Epidemiology

UC is a global disease with increasing incidence and prevalence worldwide and with different frequencies dependent on age, ethnical background and geographic localisation. Prevalence rates for UC range from 90 to 505 per 100,000 persons in Northern Europe and Northern America [1–3]. Among Caucasians the highest annual incidence of UC is 24.3 per 100,000 person-years in Europe and 19.2

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per 100,000 person-years in North America [2–4]. The disease is less common in Eastern and Southern Europe, and at least 10 times less common in Asian, African and Oriental populations. Rising incidence and prevalence have also been shown for these ethnic groups, suggesting additional environmental and lifestyle effects on the pathogenesis of UC [2,5]. The female to male ratio for UC differs between 0.51 and 1.58 indicating that UC is not sex specific [3]. Any age group from infants to the elderly can be affected, but the peak age of onset is between 15 and 30 years with a second but smaller peak between 50 and 70 years [5]. 20% to 30% of patients with UC and CrD disease have the onset of their symptoms below the age of 18, although diagnosis is often delayed.

2.1. Aetiopathogenesis

Although the precise aetiopathogenesis of UC is unknown, several immunological, genetic and environmental factors contributing to the disease have been identified. During the last years the focus of research shifted to the interplay between the environment (mainly the intestinal flora) and the defence mechanisms of the intestinal barrier (mainly the mucus layer and the mucosal immune system) [6]. UC can be considered as an immune-mediated disorder that develops in genetically predisposed individuals because of dysregulated immune responses against intraluminal antigens [7]. In a recent meta-analysis of genome-wide association studies for CrD and UC, 163 IBD-associated loci were identified. Many of them are associated with both UC and CrD. These regions contain candidate genes for a variety of functions like autophagy, microbe recognition, lymphocyte signalling, response to endoplasmic reticulum stress, cytokine signalling and others [8]. The lower concordance rate in monozygotic twins of 15% in UC compared with 30% in CrD indicates that genetic contribution in UC is weaker than in CrD, and environmental factors crucially contribute to disease and particularly to the rising incidence of UC worldwide [9]. Especially, a change to a Western lifestyle is associated with an increased risk of UC [3]. Interestingly, children from persons emigrated from an area of low prevalence to one of high prevalence showed an increased risk of UC compared to the immigrants itself suggesting that environmental factors during infancy and early childhood affecting the developing immune system and microbiota ("hygiene hypothesis") are crucial in UC development [3,10]. A diet high in saturated, milk-derived fat, as it is typically in Western-style diets, can change the composite of intestinal flora leading to an increased incidence of colitis in IL10$^{-/-}$ but not wild-type mice [11].

Table 1
Diagnostic features of ulcerative colitis.

	Feature
Clinical features (symptoms should be present for at least 4 weeks)	• Diarrhoea • Gross or occult rectal bleeding • Abdominal pain with or around time of defecation • Exclusion of intestinal infection (enteric pathogens, e.g. *Salmonella, Shigella, Yersinia, Campylobacter, E coli 0157:H7, Clostridium difficile*)
Laboratory features	• Iron deficiency anaemia • Thrombocytosis • Hypalbuminemia • Autoantibodies (GAB, atypical or perinuclear ANCA) • Elevated faecal calprotectin
Endoscopic features	• Diffuse, continuous involvement of the mucosa starting at the rectum and extending continuously proximally to a variable extent • Loss of visible vascular pattern • Loss of haustral folds • Mucosal erosions and mucosal friability (bleeding when touched by endoscope) or spontaneous bleeding and ulceration • Oedematous, erythematous appearance of the mucosa • Pseudopolyps with long-standing UC • Mucopurulent exudates
Histological features	• Increased mononuclear inflammation in the lamina propria (plasmacytosis) • Mucin depletion • Goblet cell depletion • Crypt distortion, branching and atrophy • Crypt abscesses

Table 2
UC types according to the localisation the inflammation, symptoms and signs of UC at presentation.

Type of UC	Prevalence at presentation in adult-onset IBD	Prevalence at presentation in childhood-onset IBD [28]
Proctitis	40–50%	1.4%
Left-side colitis (up to flexura sinistra)	30–40%	16%
Pancolitis (in rare cases with additional backwash ileitis)	25–30%	82%
Symptoms and signs		
Diarrhoea	70–90%	
Abdominal pain	30–70%	
Weight loss	35–45%	
Rectal bleeding	50–90%	
Growth impairment in children	5%	
Extraintestinal manifestation	2–15%	

2.2. Diagnostic criteria

Diagnosis of UC is based on medical history and clinical evaluation and then confirmed by laboratory, radiologic, endoscopic, histologic and serological findings. The most important diagnostic criteria are listed in Table 1. Patients with UC can be classified according to disease extend, disease severity, age of onset, extraintestinal manifestations and genetic markers [12]. Before making the diagnosis, infective, ischemic and irradiation causes of colitis must be excluded. Lennard-Jones [13] suggested the following criteria for the diagnosis of UC: Continuous mucosal inflammation without granulomata, always involving the rectum and extending continuously in a various degree to a part or the whole colon (Table 2). There are several definitions or criteria used to classify patients with UC [14–17]. The diagnosis of UC relies on the presence of (a) bloody diarrhoea with negative stool cultures and (b) endoscopic evidence of diffuse, continuous mucosal inflammation involving the rectum and extending to a point more proximal in the colon. However, a commonly accepted catalogue of well defined criteria or a point score for classification of UC does not exist. Abnormalities like complex or fistulising anal lesion, involvement of the upper gastrointestinal tract, skip lesions or granulomata are highly suggestive of CrD.

The category IBD unclassified (IBDU) is applied for the 5–10% of IBD patients in whom no definite diagnosis (UC or CrD) can be made. In contrast, the term indeterminate colitis should used only by the pathologist when he is not able to make a definite diagnosis on the basis of the colectomy specimen.

2.3. Medical history and clinical manifestations

The anamnesis should include clinical symptoms (Table 1) suggestive of IBD and family history (first-degree relatives of patients with UC have an increased, 10–15-fold risk for IBD). Clinically, UC is characterised by bloody diarrhoea and chronic abdominal pain [18]. Although UC is restricted to the colon by definition, nonspecific mucosal inflammation in the terminal ileum ("backwash ileitis") is found in 10–20% of the UC patients. The involvement of the upper gastrointestinal tract is a controversial issue especially in the paediatric population with UC. In contrast to adults, pancolitis in children

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